ADDomer: Thermostable synthetic self-assembling multiepitope virus-like particle for next-generation vaccines

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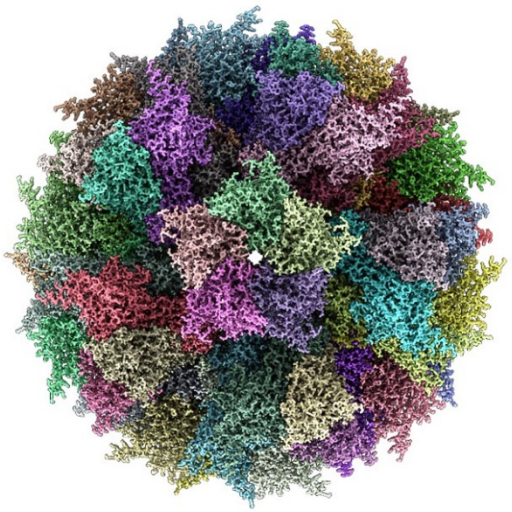
Host institution: University of Bristol
CASE partner: Imophoron Ltd



ADDomer vaccine platform by Cryo-EM

Project description:
Infectious diseases continue to plague and decimate populations world-wide, as exemplified by the COVID-19 pandemic, wreaking havoc to communities and economies world-wide. Among the means at our disposal to counter this threat, vaccination has proven to be exceptionally powerful: SARS-CoV-2 has been curbed, small-pox eradicated, measles, polio and tetanus contained in the world by vaccination. Nonetheless, severe threats continue to challenge human health, notably from viruses including Chikungunya, Zika and Dengue, that have adapted and emerged as new diseases or pathogenic strains. Originally confined to sub-saharan habitats, these pathogens are emerging as a threat also to developed countries, spread by the tiger mosquito which is increasingly present in the Northern hemisphere. Ideally, a vaccine will be safe, non-replicative, efficient, and tuneable. Moreover, it will be easily produced at industrial scale. Recombinant virus-like particles (VLPs) can be ideal candidates to address these requirements and therefore hold enormous promise in the vaccine field.

In this proposal, we will use ADDomer, a versatile, designer antigen-presenting platform we developed [1-3]. ADDomer originates from a single component of Adenovirus, the penton base protein. Engineered penton base proteins spontaneously form exceptionally stable synthetic virus-like particles in vitro, which are highly soluble and safe as they contain no genetic material. This innovative ADDomer scaffold is uniquely suited to display on a single particle hundreds of pathogenic epitopes and protein domains which are inserted into flexible, variable loops present on the ADDomer surface. In the project here proposed, we will combine world-leading expertise in synthetic biology and biodesign (Berger) with protein engineering and cryo-electron microscopy (Schaffitzel) in the new Max Planck Bristol Centre for Minimal Biology to achieve a step-change in the potency of our ADDomer technology. We are joined in our effort by our industrial collaborator (Garzoni) at Imophoron Ltd, our award winning start-up developing next-generation vaccine platforms [4]. Building on this powerful synergy, we will utilize a range of biochemical, biophysical, structural and engineering techniques to design, create, characterize, produce and roll-out highly effective next-generation ADDomer-based therapeutics to combat human infectious disease.

References

[1] Vragnieau C, Bufton JC et al. Synthetic Self-assembling ADDomer Platform for Highly Efficient Vaccination by Genetically-encoded Multi-epitope Display. Science Advances 5(9):eaaw2853, doi: 10.1126/sciadv.aaw2853 (2019)

[2] Sari-Ak D, Bufton J et al. VLP-factory and ADDomer: Self-assembling Virus-Like Particle (VLP) Technologies for Multiple Protein and Peptide Epitope Display. Current Protocols 2021, 2(3):e55. doi: 10.1002/cpz1.55 (2021)

[3] Buzas D, Bunzel HA et al. Antibodies generated in vitro and in vivo elucidate design of a thermostable ADDomer COVID-19 nasal nanoparticle vaccine. bioRxiv 2023.03.17.533092. doi: 10.1101/2023.03.17.533092 (2023)

[4] https://www.imophoron.com/

Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.